

Citation:

Solfrizzi V, D'Introno A, Colacicco AM, Capurso C, Del Parigi A, Baldassarre G, Scapicchio P, Scafato E, Amodio M, Capurso A, Panza F; Italian Longitudinal Study on Aging Working Group. Alcohol consumption, mild cognitive impairment and progression to dementia. *Neurology*. 2007 May 22; 68 (21): 1,790-1,799.

PubMed ID: [17515541](#)

Study Design:

Prospective Cohort Study

Class:

B - [Click here](#) for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

The authors sought to estimate the possible impact of alcohol consumption on the incidence of mild cognitive impairment (MCI) and its progression to dementia in a large Italian population-based sample.

Inclusion Criteria:

- Subjects in this study had to be enrolled in the Italian Longitudinal Study on Aging
 - 65-84 years of age
 - Residents of one of eight municipalities: Genova, Segrate (Milano), Selvazzano-Rubano (Padova), Impruneta (Firenze), Fermo (Ascoli Piceno), Napoli, Casamassima (Bari) and Catania
 - Willing to undergo an extensive baseline investigation, including interviews, physical exams, and laboratory tests, to identify the presence of cardiovascular disease (ischemic heart disease, hypertension, congestive heart failure, arrhythmia, intermittent claudication), diabetes, impaired glucose tolerance, thyroid dysfunction, dementia, parkinsonism, stroke, and peripheral neuropathy, as well as assess physical and mental functional status
- Informed consent was obtained for all subjects according to local institutional guidelines.

Exclusion Criteria:

- Being <65 or >84 years of age
- Demented at baseline
- Refusal to perform MMSE and/or BSRT (neuropsychological tests)
- Unknown or doubtful educational level.

Description of Study Protocol:

Recruitment

- The subjects of this study were enrolled in a larger study, the ILSA, promoted by the Italian National Research Council–CNR-Targeted Project on Aging
- Subjects aged 65 to 84 years, independent or institutionalized, were randomly selected from the electoral rolls of eight Italian municipalities, after stratification for age and gender.

Design

Prospective cohort study with 3.5 years of follow-up

Dietary Intake/Dietary Assessment Methodology

- Food-frequency questionnaires (FFQ) were completed/collected in 1992 in order to obtain information on alcohol consumption. Participants were asked how much beer or wine they had consumed per day in the previous year. The amount consumed was quantified according to three categories:
 - “Two fingers” to half a glass (equal to 0.125L)
 - Two glasses (equal to 0.25L)
 - Four glasses (equal to 0.50L)
- Data on superalcoholic beverage was collected by asking about “shots” of spirits consumed in the previous year, according to three frequency categories:
 - Number of times per day
 - Number of times per month
 - Number of times per year
- Subjects were also asked when they had begun to drink, and how much beer or wine per day they had consumed ever since to evaluate among drinkers who never interrupted their drinking habits, who interrupted their drinking habits during the preceding five years (current), and who interrupted their drinking habits before the preceding five years (former).

Statistical Analysis

- Rate of incident mild cognitive impairment (MCI) and its progression to dementia associated with alcohol consumption assessed using Cox proportional hazards regression analysis
- Alcohol was assessed as a continuous (number of drinks per day) and as a categorical variable (no alcohol intake, no more than one drink per day, one or more drinks, but no more than two drinks per day, at least two drinks per day). “No alcohol intake” was used as the reference
- Proportional hazards assumptions were checked by plotting log-minus-log curves. The rate of MCI in NCI individuals and the progression to dementia in patients with MCI associated with specific classes of alcoholic beverage were analyzed in separate regression models
- For each individual, the amount of alcohol intake deriving from wine, beer, and superalcoholic beverages was expressed in the number of drinks, controlled for alcohol deriving from other sources within each category of total alcohol intake
- A possible linear relationship was evaluated between total alcohol intake, wine and beer beverages (considered as continuous variables) and rate of MCI in NCI individuals and rate of progression to dementia in patients with MCI who reported in the questionnaires to be current or former drinkers (linear models)
- A possible quadratic relationship was evaluated between each type of alcoholic beverage and rate of incident MCI in NCI subjects and rate of progression to dementia in patients with

MCI, squaring each type of alcoholic beverage variable (X, linear term) after centering it on median consumption (X², quadratic term) by a polynomial model

- All analyses were controlled for age and gender
- Analyses were adjusted for possible confounders: Education, cigarette pack-years, Coronary Artery Disease (CAD), type 2 diabetes, hypertension, stroke, and total cholesterol (TC)
- SAS statistical software version 9.1 (SAS Institute Inc, Cary, NC) was used for all analyses.

Data Collection Summary:

Baseline (data collected in 1992)

- CAD (myocardial infarction and angina pectoris), hypertension, type 2 diabetes mellitus, and stroke were identified with a two-phase procedure. In Phase 1, a screening questionnaire, a series of brief screening tests to identify suspect cases for further investigation, and a clinical evaluation were administered to each subject; in Phase 2, suspected cases were confirmed with a standardized clinical examination by a certified geriatrician, neurologist or internist
- A screening questionnaire included information on demographic characteristics, body weight and weight history, smoking habits, and current use of medications (including inspection of the drugs by the interviewer)
- Blood samples were obtained after a 13-hour overnight fast; serum TC concentration was determined
- Based on self-reports, smoking habits were categorized as “ever” or “never,” based on self-reports and the variable “cigarette pack-years” [years smoked * usual number of cigarettes smoked with 20 cigarettes per pack] was generated to represent the total smoking exposure.

Dependent Variables

- Dementia
- Mild cognitive impairment (MCI).

Independent Variable

Alcohol consumption.

Control Variables

- Analyses were controlled for age and gender
- Adjustment for possible confounders included: Education, cigarette pack-years, CAD, type 2 diabetes, hypertension, stroke and TC.

Description of Actual Data Sample:

- *Initial N:*
 - Of a total of 5,632 elderly subjects enrolled in the cohort in 1992, 4, 521 agreed to participate in this study
 - Of these 4,521, 1,558 were excluded based on inclusion/exclusion criteria leaving 2,965 (1,589 males and 1,374 females)
 - Of the 2,965, 1,445 subjects completed follow-up (815 males and 630 females)

- *Final N:*
 - 1,445
 - 15,341 person-years of follow-up
 - Median follow up=3.5 years
- *Age:* 65-84 years
- *Ethnicity:* Italian
- *Location:* Residents of one of eight municipalities:
 - Genova
 - Segrato (Milano)
 - Selvazzano-Rubano (Padova)
 - Impruneta (Firenze)
 - Fermo (Ascoli Piceno)
 - Napoli
 - Casamassima (Bari)
 - Catania.

Summary of Results:

- Patients with MCI who were moderate drinkers (i.e., those who consumed less than one drink per day (approximately 15g of alcohol), had a lower rate of progression to dementia than abstainers (hazard ratio [HR] 0.15; 95% CI 0.03 to 0.78)
- Moderate drinkers with mild cognitive impairment who consumed less than one drink per day of wine showed a significantly lower rate of progression to dementia than abstainers (HR 0.15; 95% CI 0.03 to 0.77)
- There was no significant (NS) association between higher levels of drinking (at least one drink per day) and rate of progression to dementia in patients with mild cognitive impairment vs. abstainers
- NS associations were found between any levels of drinking and the incidence of mild cognitive impairment in non-cognitively impaired individuals vs. abstainers.

Author Conclusion:

In patients with MCI, up to one drink per day of alcohol or wine may decrease the rate of progression to dementia.

Reviewer Comments:

(Including this because paper said "described elsewhere") Description of the ILSA [from: Aging (Milano). 1994 Dec; 6 (6): 464-473.]

- *The Italian Longitudinal Study on Aging (ILSA) is a population-based, longitudinal study of the health status of Italians aged 65-84 years. The main objectives of ILSA are the study of the prevalence and incidence rates of common chronic conditions in the older population, and the identification of their risk and protective factors. ILSA is also designed to assess age-associated physical and mental functional changes*
- *A random sample of 5,632 individuals, stratified by age and gender using the equal allocation strategy, was identified on the demographic lists of the registry office of eight municipalities: Genova, Segrato (Milano), Selvazzano-Rubano (Padova), Impruneta*

(Firenze), Fermo (Ascoli Piceno), Napoli, Casamassima (Bari) and Catania

- *An extensive investigation, including interviews, physical exams, and laboratory tests, was conducted at baseline to identify the presence of cardiovascular disease (ischemic heart disease, hypertension, congestive heart failure, arrhythmia, intermittent claudication), diabetes, impaired glucose tolerance, thyroid dysfunction, dementia, parkinsonism, stroke, and peripheral neuropathy, as well as assess physical and mental functional status*
- *The baseline examination was carried out between March 1992 and June 1993; a second comprehensive examination will begin in March 1995. An interim hospital discharge data survey and a mortality survey are currently ongoing to assess the hospitalization rate and the cause-specific mortality rate in this study cohort.*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

- | | | |
|----|---|-----|
| 1. | Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies) | Yes |
| 2. | Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about? | Yes |
| 3. | Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice? | Yes |
| 4. | Is the intervention or procedure feasible? (NA for some epidemiological studies) | Yes |

Validity Questions

- | | | |
|------|---|-----|
| 1. | Was the research question clearly stated? | Yes |
| 1.1. | Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified? | Yes |
| 1.2. | Was (were) the outcome(s) [dependent variable(s)] clearly indicated? | Yes |
| 1.3. | Were the target population and setting specified? | Yes |
| 2. | Was the selection of study subjects/patients free from bias? | Yes |
| 2.1. | Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study? | Yes |
| 2.2. | Were criteria applied equally to all study groups? | Yes |
| 2.3. | Were health, demographics, and other characteristics of subjects described? | Yes |

2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	Were study groups comparable?	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	N/A
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	No
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	Was method of handling withdrawals described?	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	N/A
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	Was blinding used to prevent introduction of bias?	???
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	???
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	No

5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were intervening factors described?	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	No
6.6.	Were extra or unplanned treatments described?	No
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	N/A
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	Were outcomes clearly defined and the measurements valid and reliable?	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	Was the statistical analysis appropriate for the study design and type of outcome indicators?	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes

8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	Yes
9.	Are conclusions supported by results with biases and limitations taken into consideration?	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	Is bias due to study's funding or sponsorship unlikely?	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes